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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/692,303	10/23/2003	Thomas Primiano	02-1133-C	7346

7590 04/27/2007

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EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	**PAPER NUMBER**
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/692,303	PRIMIANO ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *1-7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/1/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed 2/26/07 on has been entered.

2. Claims 1-9 are all the pending claims for this application.

3. Claim 8 was amended in the Response of 2/26/07. Applicants identify written support for the amendment to recite "for treating a tumor cell that expresses L1CAM" in [0048, 0050 and Example 1] of the specification. The amendment to recite that the antibody is "unconjugated" is supported at [0012 and Example 1] of the specification. The amendment to recite the "wherein" clause raises an issue of new matter as discussed infra.

4. Claims 1-7 are withdrawn form consideration.

5. Claims 8 and 9 are all the pending claims under examination.

Information Disclosure Statement

6. The information disclosure statement filed 2/26/07 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other

information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

7. The IDS filed 3/1/07 is a virtual duplicate of the IDS of 2/26/07 and copies of the cited references have been considered and entered.

Withdrawal of Rejections

Claims - 35 USC § 112, first paragraph

Enablement

8. The rejection of Claims 8 and 9 under 35 U.S.C. 112, first paragraph, as lacking enablement for a reasonable number of therapeutically effective L1CAM antibodies is withdrawn in view of Applicant's allegations beginning on the bottom of p. 7 to the top of p. 9 of the Response of 2/26/07.

Applicants reiterate the Examiner's analysis of the Primiano and Arlt references describing the proliferation inhibitory effects of the unconjugated UJ127, 5G3, L1-11A and chCE7 antibodies on various tumor cell lines in vitro, and as further evidenced by Example 1 in the specification. Further, Arlt demonstrates the growth inhibitory effects of the L1-11A and chCE7 antibodies in vivo in a mouse model for a human ovarian cancer.

Claims - 35 USC § 102

9. The rejection of Claims 8 and 9 under 35 U.S.C. 102(b) as being anticipated by Hoefnagel et al. (European J. Nuclear Medicine 28:359-368 (March 2001) is withdrawn in view of the amendment of Claim 8 to recite "an unconjugated" antibody.

Applicant argues that Hoefnagel does not teach or suggest the use of an unconjugated anti-L1CAM antibody or L1CAM-binding fragment (pp. 4-5 of the Response of 2/26/07). Applicants argue that Hoefnagel uses the chCE Mab for targeted radioimmunotherapy. Applicant's arguments and the amendment have been considered and are found persuasive.

10. The rejection of Claims 8 and 9 under 35 U.S.C. 102(b) as being anticipated by Carrel et al. (Nuclear Medicine Biol. 24(6):539-546 (August 1997) is withdrawn in view of the amendment of Claim 8 to recite "an unconjugated" antibody.

Applicant argues that Carrel does not teach or suggest the use of an unconjugated anti-LICAM antibody or LICAM-binding fragment (p. 5, ¶3 of the Response of 2/26/07). Applicants argue that Carrel uses the chCE Mab for targeted radioimmunotherapy. Applicant's arguments and the amendment have been considered and are found persuasive.

11. The rejection of Claims 8 and 9 under 35 U.S.C. 102(b) as being anticipated by Mujoo et al. (J. Biol. Chem. 261:10299-10305 (1986) as evidenced by Wolff et al (J. Biol. Chem. 263:11943-11947 (1988)) is withdrawn in view of the amendment of Claim 8 to recite "an unconjugated" antibody.

Applicant argues that Mujoo as evidenced by Wolff does not teach or suggest the use of an unconjugated anti-LICAM antibody or LICAM-binding fragment (p. 5, ¶4- p.6, ¶1 of the Response of 2/26/07). Applicants argue that neither reference alone or in

combination uses an unconjugated 5G3 Mab for targeted immunotherapy but only conjugated forms. Applicant's arguments and the amendment have been considered and are found persuasive.

12. The rejection of Claims 8 and 9 under 35 U.S.C. 102(b) as being anticipated by Patel et al. (Hybridoma 10:481-491 (1991)) is withdrawn in view of the amendment of Claim 8 to recite "an unconjugated" antibody and the intended use for "treating a tumor cell that expresses L1CAM."

Applicant argues that Patel does not teach or suggest the use of an unconjugated anti-LICAM antibody or L1CAM-binding fragment for the treatment of cancer (p. 6, ¶2). Applicant's arguments and the amendment have been considered and are found persuasive.

35 USC § 103

13. The rejection of Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wolff et al. (J. Biol. Chem. 263:11943-11947 (1988)) in view of Cleland et al. (J. Pharm. Sci. 90:310-321 (2001)) is withdrawn in view of the amendment of Claim 8 to recite "an unconjugated" antibody and the intended use for "treating a tumor cell that expresses L1CAM."

Applicant argues that Wolff does not teach or suggest the use of an unconjugated anti-L1CAM antibody or L1CAM-binding fragment for the treatment of

cancer (p. 7, ¶1). Applicant's arguments and the amendment have been considered and are found persuasive.

Rejections Maintained

Claims - 35 USC § 112, first paragraph

Enablement

14. The rejection of Claims 8 and 9 under 35 U.S.C. 112, first paragraph, because the specification, as lacking enablement for using any L1CAM antibody to inhibit proliferation of just any cancer cell is maintained because the delivery of high molecular weight molecules, i.e., antibodies, to cancers in vivo is unpredictable.

Claims 8 and 9 are drawn to treating any L1CAM-expressing tumor cell.

Applicant's arguments on pp. 9-10 of the Response of 2/26/07 have been considered but are not persuasive. Applicants argue that Herceptin® was a well-established in vivo antibody therapy at the time of application filing, and irrespective of the cited art references discussing unpredictability of immunotherapeutics for cancer therapy (Jain, Chaterjee and Gura), the claims are enabled for treating any L1CAM-expressing tumor with any L1CAM antibody.

The Examiner respectfully disagrees and submits that at the time of application filing, only a limited number of monoclonal antibodies were FDA approved for clinical use, and of those, even fewer were intended for cancer therapy (see list of oncologics in Table 1 of Reichert et al. (Nat. Biotech. 23(9):1073-1078). Applicants correctly observe that they are not required provide human clinical data, but as Reichert points out, the

leap from bench to bedside is unpredictable. Further, only a limited number of in vivo studies using unconjugated L1CAM antibodies have been performed to substantiate the tumor targeting potential of the respective antibody (see Arlt et al. (of record)) and Izumoto et al. (Can Res. 56:1440-1444 (1996); cited in the IDS of 3/1/07) discussed infra. Finally, the approved antibodies for in vivo use are generally chimeric or humanized monoclonals and the claims are drawn to treating any tumor with any kind of L1CAM antibody. Applicants have not limited the claims to overcome the outstanding rejection, or in the alternative, provided extrinsic evidence supporting the breadth of scope, therefore the rejection is maintained.

Claims-35 USC § 103

15. The rejection of Claim 8 under 35 U.S.C. 103(a) as being unpatentable over Rathjen et al. (EMBO J. 3:1-10 (1984)) in view of Cleland et al. (J. Pharm. Sci. 90:310-321 (2001)) is maintained.

Applicant argues on p. 7, ¶1 of the Response of 2/26/07 that "the only process cited in the reference teaches where L1CAM protein is involved in cell adhesion... Rathjen does not teach that L1CAM plays a role in cell proliferation." And Rathjen does not teach using an unconjugated antibody to treat cancer.

The Examiner submits that inasmuch as Rathjen does not teach inhibition of neuroblastoma cell proliferation with the L1CAM antibodies, Rathjen does teach inhibiting neuroblastoma cell aggregation, which is a form of treatment. In response to applicant's argument that the references fail to show certain features of applicant's

invention, it is noted that the features upon which applicant relies (i.e., treating a tumor cell with a L1CAM antibody in order to inhibit cell proliferation) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

New Grounds for Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Claim 8 recites a "wherein" clause for a negative proviso which is new matter.

Claim 8 has been amended to recite the ":wherein" clause where "the antibody is not conjugated to a radionucleotide or toxin."

The specification does not teach or suggest the negative proviso much less the terms for a "radionucleotide" or a "toxin". The Examiner's search of the specification did not identify any support for the newly amended claim.

Further and pursuant to MPEP 2173.05(i) "Any negative limitation or exclusionary proviso must have basis in the original disclosure."

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claim 8 is rejected under 35 U.S.C. 102(b) as being anticipated by Izumoto et al. (Can Res. 56:1440-1444 (1996); cited in the IDS of 3/1/07).

The interpretation of Claim 8 is of record and discussed supra.

Izumoto teaches the inhibition of L1-mediated cell migration of rat C6 glioma by anti-L1 antibodies. The antibodies were rabbit anti-rat L1 antibodies, which recognized the IgGC2 domain, the FN type III domain, and the IC domain of L1, respectively. Izumoto reads on and anticipates the claim because the treatment is not limited to any endpoint, and thus encompasses inhibiting cell migration.

Conclusion

18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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